August 18, 2021

HEALTHCARE/BIOTECHNOLOGY

Women Leaders in Biotechnology Inspire from Kendall Square

Spotlight on Female Innovators in Biotech at MIT

SUMMARY

We hosted our inaugural event with Massachusetts Institute of Technology (MIT) highlighting women in biotechnology. Professor Robert S. Langer graciously provided an introduction to our virtual event by sharing examples of female entrepreneurs, industry leaders, and academic scientists. The Langer Lab at MIT has spun-out numerous female-led biotech startups, such as EpiBone led by Co-Founder/CEO Nina Tandon. Professor Langer also spoke about his role as Co-Founder of Moderna (MRNA), where he noted female R&D leaders Melissa Moore and Kerry Benenato. Professors Angela Koehler, Li-Huei Tsai, and Paula Hammond presented on their academic research, and Junghae Suh presented on BIIB's gene therapy pipeline. Additionally, BioCentury Senior Editor Karen Tkach Tuzman moderated a panel discussion with women across diverse backgrounds that focused on empowering women to pursue careers in biotechnology. MIT's Future Founders Initiative has made progress toward closing the gender gap. Video replay (passcode: aj5#*M?^).

KEY POINTS

- Professor Langer provided numerous examples of female entrepreneurs and academic scientists from MIT. Company examples include Lyndra Therapeutics, PureTech Health, Daré Bioscience (DARE), Lyra Therapeutics (LYRA), EpiBone, Tara Biomedical, Arsenal Medical, and Glympse Bio. Academic scientists include Professors Ana Jaklenec, Ann Graybiel, Sangeeta Bhatia, Dina Katabi, and Regina Barzilay. Professor Langer discussed his role as Co-Founder of MRNA, and noted Kerry Benenato who participated on our panel. Professor Langer also offered advice to aspiring entrepreneurs.
- MIT faculty presentations included: Professor Angela Koehler on expanding the repertoire of druggable targets by applying her proprietary small molecule microarray platform; Professor Li-Huei Tsai on modeling human neurological disorders and targeting disease risk genes using stem-cell derived 3D co-cultures; and Professor Paula Hammond on electrostatic assemply for targeted nucelic acid and combination nano-therapies. MIT alumna and Rice University Professor Junghae Suh presented on BIIB's gene therapy pipeline for neuroscience.
- BioCentury Senior Editor Karen Tkach Tuzman moderated a panel discussion with women leaders in biotechnology, including Kerry Benenato, Vanessa Bhark, Ginger Johnson, Susan Langer, and Nina Tandon. Our panelists described their diverse backgrounds and experiences, and focused on the evolving landscape for women pursuing biotech careers. Although more changes are required for further progress toward equal opportunity and representation, our panelists expressed optimism for future generations of women in biotech and offered advice.
- MIT's Future Founders Initiative provides funding opportunities to female founders, which was formed in response to the MIT report on 40 missing biotech companies. According to a BCG report, only 2% of female-led startups received VC funding, but these founders generated 10% more revenue in 5-years compared to men. We believe that efforts to narrow the gender gap should help to eliminate these opportunity costs and ultimately drive valuable innovation.

Jay Olson, CFA
212-667-8126
Jay.Olson@opco.com

Matthew Hershenhorn
212-667-7590
Matthew.Hershenhorn@opco.com

Cheng Li, Ph.D., CFA
212-667-7187
Cheng.Li@opco.com

Disseminated: August 18, 2021 16:26 EDT; Produced: August 18, 2021 16:26 EDT

For analyst certification and important disclosures, see the Disclosure Appendix.

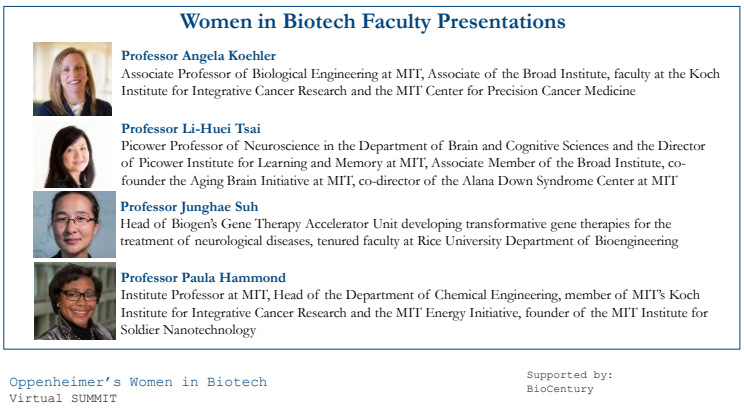
Introduction

Professor Robert S. Langer, Sc.D., Dept. of Chemical Engineering, MIT

Professor Robert S. Langer, David H. Koch Institute Professor of Chemical Engineering at Massachusetts Institute of Technology (MIT), graciously provided an introduction to our virtual event highlighting women in biotechnology. Professor Langer began by referencing several examples of female entrepreneurs and leaders at biotechnology companies which have spun-out of the Langer Lab at MIT or in which Professor Langer has been involved. Examples include: Lyndra Therapeutics, led by Chairwoman Catherine B. Reynolds, Executive-Chairwoman Amy Schulman, CEO Patricia Hurter, and COO Jessica Ballinger; PureTech Health, led by Founder/CEO/Director Daphne Zohar; Daré Bioscience (DARE), led by Founder/CEO Sabrina Johnson; Lyra Therapeutics (LYRA), led by CEO/Director Maria Palasis; EpiBone, led by Co-Founder/CEO Nina Tandon and Co-Founder/Director Gordana Vunjak-Novakovic; Tara Biomedical, led by CEO Misti Ushio and also cofounded by Gordana Vunjak-Novakovic along with Milica Radisic; and Arsenal Medical, led by CEO Upma Sharma. Professor Langer also provided examples of leading female scientists who are working in exciting academic areas at MIT, including: Professor Ana Jaklenec, who is researching single-administration vaccines and nutrition delivery; Professor Li-Hue Tsai, who is researching neural circuitry approaches to neurological disorders and collaborating with Professor Langer on creating the miBrain-chip platform; Professor Ann Graybiel, who also is working in neuroscience and is collaborating with Professor Langer on developing devices for the brain; Professor Sangeeta Bhatia, who is researching computer science approaches to biomedical research and cofounded Glympse Bio, which is led by female CEO Caroline Loew; Professor Dina Katabi, who is working on digital health applications; and Professor Regina Barzilay, who is working on machine learning models for diagnoses and drug discovery. Professor Langer also is a Co-Founder of Moderna (MRNA), where he noted key female leaders CSO Melissa Moore and VP of R&D Kerry Benenato.

We asked Professor Langer about the challenges and rewards of starting a biotechnology company, and he suggested that running the business becomes the primary challenge following scientific rationale, so hiring the right CEO, consulting with legal experts on IP, and finding loyal investors become key prerogatives, and the reward is helping patients. He also advised that entrepreneurs only start a biotech company when completely ready. We then asked Professor Langer about what he views as the most exciting areas in biomedical research today, and he mentioned tissue engineering to treat paralysis, hearing loss, and cardiovascular diseases, in addition to technologies that could help developing countries such as new vaccines, oral drug delivery systems, and nutrition, which are all among the current focus areas of the Langer Lab at MIT.

Exhibit 1. MIT Women in Biotech event faculty presentations



Source: Oppenheimer Research.

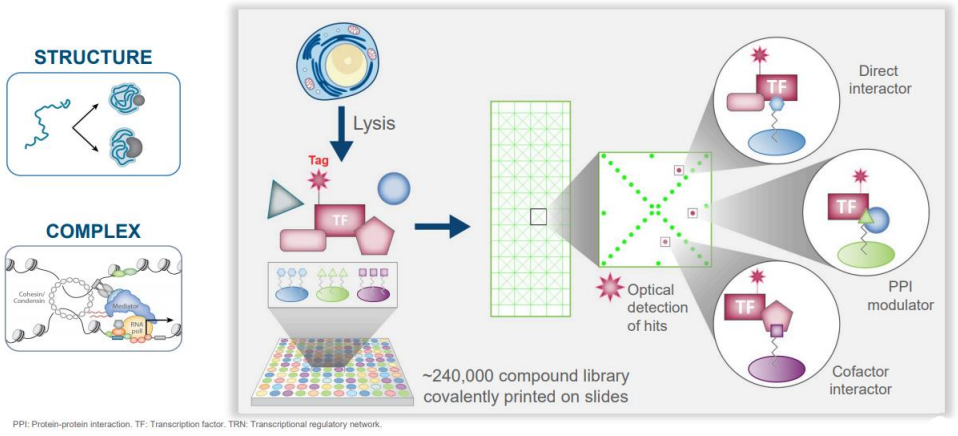
Professor Angela Koehler, PhD

Expanding the Repertoire of Druggable Targets

Transcription factors are essential in regulating the gene expression network to establish cell identification and to maintain physiological functions of the cell. Not surprisingly, many transcription factors and their corresponding transcriptional regulatory networks are hijacked by cancer cells to promote their uncontrolled proliferation and metastasis. Therefore, transcriptional factors represent an ideal class of therapeutic targets in oncology. Despite their broad therapeutic promise, there are major challenges in designing and developing molecules targeting transcription factors as many of them are considered to have “undruggable” structures.

Dr. Koehler and her team are developing a general approach to small-molecule probe discovery for transcription factors based on a high-throughput binding assay platform called small molecule microarray (SMM; Exhibit 2). Dr. Koehler and her team use cell lysate to conduct the SMM screen, in order to maintain the target protein structure under physiological conditions as well as its interacting components. Using this unbiased approach, hits identified in the SMM screens may bind directly to the transcription factor of interest or bind to its interactors to either activate or suppress the transcriptional network. Hits can be subsequently optimized with ideal clinical PK/PD characteristics for clinical studies or they can be endowed with novel properties such as acting as protein degraders to modulate transcriptional networks in different ways.

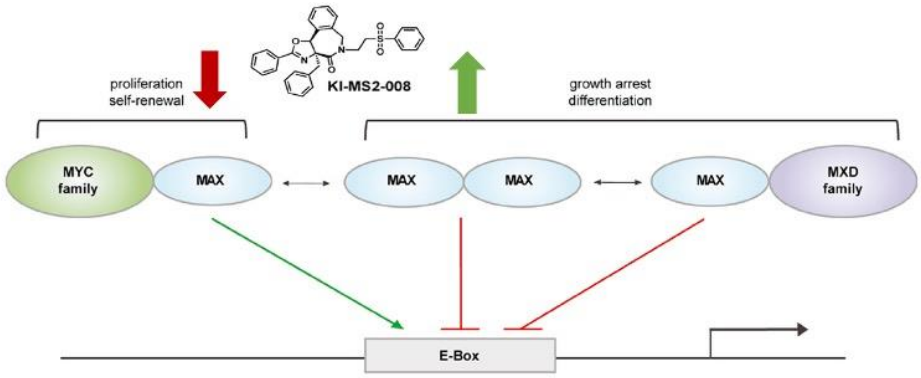
Exhibit 2. Small molecule microarray (SMM) platform for screening transcription factors



Source: Kronos Bio Company Presentation

Myc is a master regulator of cell growth and survival and is deregulated in >50% of human cancers. Although Myc inhibition represents an ideal approach for cancer treatment, direct targeting of Myc has been challenging due to its undruggable structure. Myc also forms heterodimers with Max, and the Myc-Max protein complex binds to DNA regulatory regions to activate gene expression. Efforts have also focused on disrupting the Myc-Max interaction but had proved to be unsatisfactory. Leveraging the SMM platform, Dr. Koehler and the team have discovered a compound that can inhibit Myc activity by binding to Max. The candidate, KI-MS2-008, stabilizes the Max homodimer, thus shifting the dynamics of Myc-Max heterodimer and Max-Max homodimer, leading to reduced Myc protein levels and Myc-activated transcript levels (Exhibit 3). Treatment with KI-MS2-008 also suppresses tumor growth in a Myc-dependent manner in vivo. The discovery of KI-MS2-008 provides new insights into Myc modulation, demonstrating the power of the SMM platform.

Exhibit 3. KI-MS2-008 interacts with and stabilizes the Max-Max homodimer, leading to reduced Myc protein levels and Myc-dependent transcript levels



Source: Adapted from Struntz et al., Cell Chem Biol, 2019

Dr. Koehler also is the scientific founder of Kronos Bio (KRON), a clinical-stage biotech company focused on the discovery and development of therapeutics that modulate historically "undruggable" targets leveraging the SMM platform. KRON's lead programs include SYK inhibitors in AML patients carrying certain mutations, and a CDK9 inhibitor targeting MYC-amplified tumors.

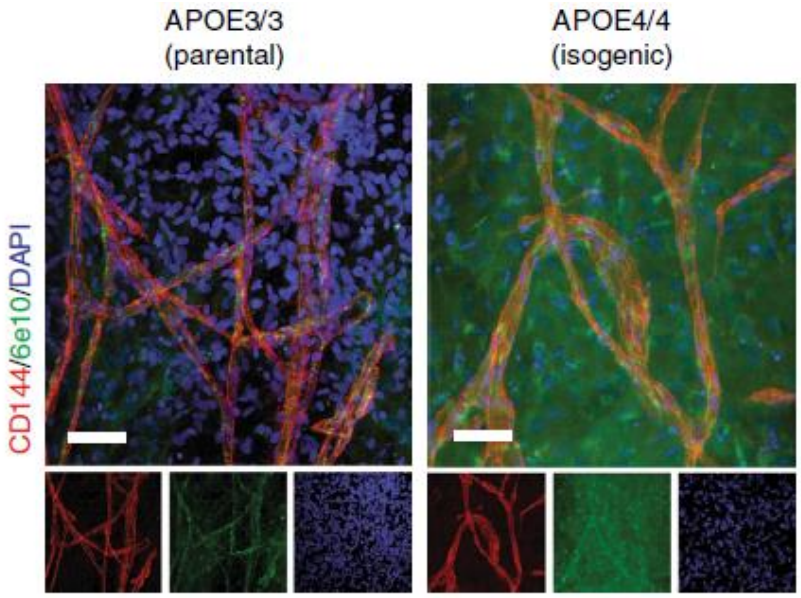
Professor Li-Huei Tsai, PhD

Modeling human neurological disorders and targeting disease risk genes using stem-cell derived 3D co-cultures

Dr. Tsai's lab focuses on understanding the pathogenic mechanisms underlying neurodegenerative disorders, e.g., Alzheimer's disease (AD). Among many research areas of the lab, Dr. Tsai shared the story of using stem-cell derived 3D co-cultures representing the human blood-brain barrier to study the pathogenic mechanism of APOE4.

APOE4 is the most significant risk factor for AD development. While APOE4 carriers only represent ~15% of the general population, about 40-50% of AD patients are found to be APOE4 carriers. The pathogenic mechanism of APOE4 in AD is an area of great research interest. It has been shown that APOE4 is associated with reduced myelination, increased neuro-inflammation, and tau pathology during AD development. The majority of AD patients also exhibit a condition called cerebral amyloid angiopathy (CAA), in which patients have amyloid deposition along the cerebral vasculature. It is not known if APOE4 contributes to the CAA phenotype due to a lack of human blood-brain barrier (BBB) models. Using an iPSC-derived 3D model, Dr. Tsai's group successfully reconstructed the human BBB (iBBB) with structural and physiological properties in a dish. Utilizing this in vitro model, iBBBs generated from isogenic APOE3/3 and APOE4/4 iPSCs were treated with amyloid medium, and APOE4/4 iBBBs exhibited significantly greater amyloid accumulation along the vasculature compared to APOE3/3 iBBBs (Exhibit 4), suggesting a pathogenic role of APOE4 in CAA.

Exhibit 4: APOE4/4 iBBBs exhibit significantly higher degrees of amyloid accumulation (labeled by 6e10 in green) compared to APOE3/3 iBBBs

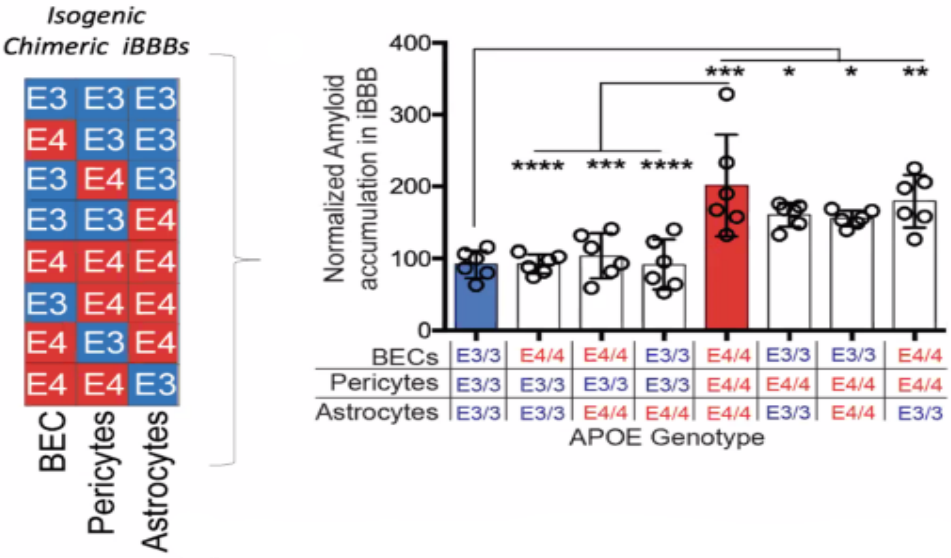


Source: Blanchard et al., Nature Med, 2020

The BBB is primarily formed by three different cell types: endothelial cells, pericytes, and astrocytes. To further characterize APOE4's contribution to the CAA phenotype by each cell type, the researchers reconstructed iBBBs with different combinations of APOE3/3 and APOE4/4 cells. Quantification of amyloid deposition with each possible combination revealed that APOE4/4 pericytes are required for increased amyloid deposition in the BBB (Exhibit 5). Mechanistically, APOE and calcineurin signaling are upregulated in APOE4 pericytes, and inhibition of calcineurin reduces APOE expression and amyloid deposition.

Interestingly, retrospective studies show that individuals chronically treated with calcineurin inhibitors to prevent organ transplant rejection have a significantly lower incidence of dementia. As many of the calcineurin inhibitors are associated with toxicity, a safer calcineurin inhibitor might represent a new approach to AD/dementia prevention.

Exhibit 5: APOE4 pericytes are necessary for CAA phenotype



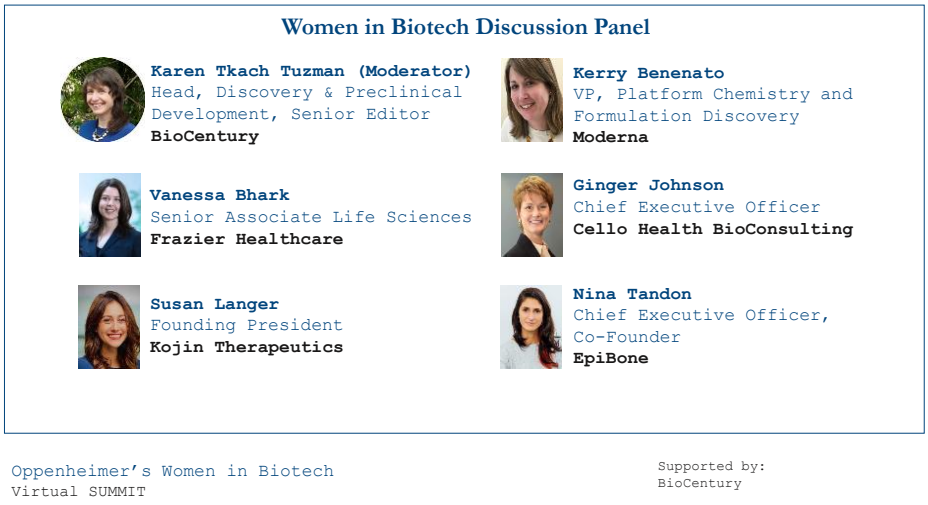
Source: Blanchard et al., Nature Med, 2020

Panel Discussion: *Women in Biotechnology*

Karen Tkach Tuzman, Senior Editor, BioCentury

Karen Tkach Tuzman, Senior Editor at BioCentury moderated a panel discussion featuring female leaders in biotechnology, including: Kerry Benenato, VP of Platform Chemistry and Formulation Discovery at MRNA; Vanessa Bhark, Senior Associate at Frazier Healthcare; Ginger Johnson, CEO of Cello Health BioConsulting; Susan Langer, Founding President of Kojin Therapeutics; and Nina Tandon, Co-Founder/CEO of EpiBone. Karen first asked our panelists to provide an overview of their backgrounds and career experiences as women in biotech. Nina cited support to transition from academia to entrepreneurship from her mentor, EpiBone Co-Founder Gordana Vunjak-Novakovic. Ginger commented that an attitude of "not being afraid to say 'no' or fail" was supported by her female mentors, which provided her with the confidence to succeed. Kerry noted that MRNA prioritizes diversity of opinions, so she feels empowered to contribute. Vanessa outlined her journey across financial, industry, and VC roles while always staying curious. Susan noted that her father, Professor Langer, encourages her independence, and that her former colleagues at BIIB were always supportive. Our panelists overlapped on pursuing a passion for life sciences despite challenges, seeking and receiving support from key mentors, and nurturing a spirit of intellectual curiosity. Karen then asked about changes from one generation to the next, and Ginger believes that conversations about supporting women in biotech are gaining traction, as evidenced by the success of the Women in Bio (WIB) Entrepreneur Center. Nina noted the recent NASDAQ board diversity rule which aims to increase representation of women on boards. Karen referenced the MIT report on 40 missing biotech companies that would have been founded by women but had not received funding, which resulted in MIT's Future Founders Initiative, and asked about how disparities could be overcome. Vanessa cited a BCG report which found that only 2% of female-led companies received VC funding, but that startups founded by women generated 10% more revenue in 5-years compared to men. Vanessa believes that the financial incentive should drive VC funding for women, and that new laws such as California SB-826 requiring female board members also help to narrow the gender gap. Finally, Karen asked about learnings from experience and advice to future women in biotech. Ginger suggested not to hesitate to be a mentor, Nina offered encouragement to pursue one's own idea, Kerry views self-belief as crucial, Susan emphasized the importance of loyalty, and Vanessa recommends finding the right environment that provides support. We thank our panelists for their unique insights.

Exhibit 6. "Women in Biotech" discussion panel moderator and participant profiles



Source: Oppenheimer Research.

Exhibit 7. Our analysis found that women are underrepresented in board, management, and founder positions vs. their male counterparts across the most recent biotech IPOs

Biotech IPOs	Board % Female	Mgmt. % Female	Founders % Female
2019	23%	13%	18%
2020	23%	21%	9%
2021	22%	20%	6%
Wt. Avg.	**23%**	**18%**	**10%**

Source: FactSet; Oppenheimer Research.

Exhibit 8. BCG found that women founders receive less funding but generate more revenue



Source: BCG.

Exhibit 9. "SHE" ETF tracks female-led companies, and is outperforming the S&P-500



Comparable Returns

	Price Change (%)		Total Return (%)		NAV Total Return (%)	
	Cum	Ann (CGR)	Cum	Ann (CGR)	Cum	Ann (CGR)
SPDR SSGA Gender Diversity Index ETF	35.42	35.42	36.96	36.96	38.33	38.46
S&P 500	32.46	32.46	34.48	34.48	--	--

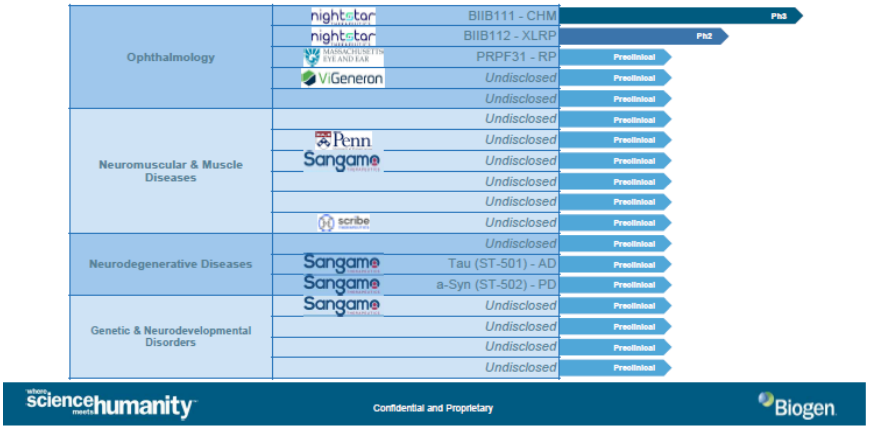
Source: FactSet.

Professor Junghae Suh, PhD

Building Biogen's Gene Therapy for Neuroscience

Dr. Suh's research focuses on AAV capsid engineering with synthetic virology for gene therapy delivery and applications in biomedicine. In 2007, Dr. Suh started her career at Rice University Department of Bioengineering where she remains on the faculty. After 12 years in academia, Dr. Suh joined Biogen in 2019 where she leads the company's Gene Therapy Accelerator Unit (GTxAU). With a specialty in CNS diseases, Biogen aims to utilize different modalities, including small molecule, biologic, gene therapy, and oligonucleotide medicine to transform patients' lives. Through both internal development and collaborations, Biogen's gene therapy pipeline covers multiple therapeutic areas, including ophthalmology, neuromuscular disease, neurodegenerative disease and other genetic disorders (Exhibit 10). The goal of the GTxAU at Biogen is to make Biogen a leader in the application of gene therapy in neuroscience.

Exhibit 10: Biogen's gene therapy pipeline



Source: Suh, MIT Women in Biotech, 2021

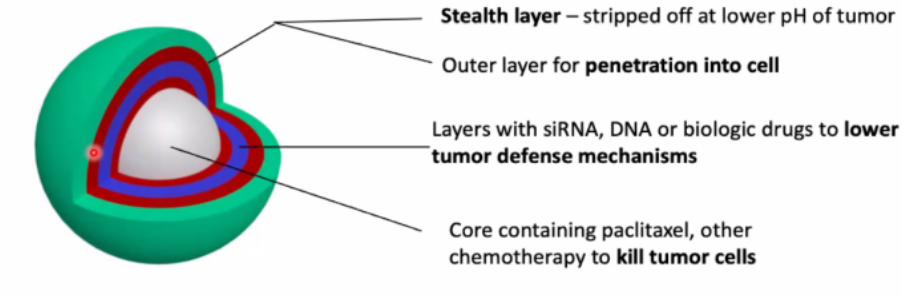
The key to utilizing gene therapy in neuroscience is to identify and solve critical rate-limiting steps in the technologies, capabilities, and development processes. At Biogen, the foundation of the gene therapy franchise covers four components: capsid, cargo, vector production, and vector performance. Biogen exploits both internal and external resources to address each of the four pillars of the gene therapy foundation. For instance, the route of gene therapy administration into the CNS is closely related to capsid and vector performance. A more desirable biodistribution of vector in the CNS often requires a more invasive administration route, and the benefit/risk ratio of each program needs to be evaluated individually. A smarter way, e.g., using machine learning-enabled systems, to design AAV capsids and a systematic method to characterize in vivo capsid tropisms might help to enhance vector performance in the clinic. With advancing gene therapy development, there are also challenges discovered along the way. One example is the finding that gene therapies for CNS are often found to be associated with dorsal root ganglion toxicity, which may be due to overexpression of the AAV cargo. A more careful selection of promoter strength, or even designing a controllable/switchable promoter, may be required. Besides capsid and vector performance, Biogen is also investing in the cargo as well as manufacturing. In 2020, Biogen formed a collaboration with Scribe Therapeutics, a private biotech company focusing on molecular engineering of CRISPR-based gene editing systems, for the development of novel genetic medicines for neurodegenerative diseases including ALS. Scribe's X-editing CRISPR system is small enough to be fitted within an AAV capsid, enabling in vivo gene editing in the CNS. Biogen also recently announced plans to build a new gene-therapy manufacturing facility with an approximately $200M investment. The new facility is expected to be operational by 2023.

Professor Paula Hammond, PhD

Electrostatic Assembly for Targeted Nucleic Acid and Combination Nano-Therapies

Professor Paula Hammond is an Institute Professor at MIT and the head of the Department of Chemical Engineering. She is a member of the National Academy of Sciences, the National Academy of Engineering, the National Academy of Medicine, and the American Academy of Arts and Sciences. The Hammond lab focuses on the self-assembly of polymeric nanoparticles using electrostatics. By coating polymer layers that have opposite charges, layer-by-layer (LbL) controlled release nanoparticles are developed for targeted delivery of cancer therapy (Exhibit 11).

Exhibit 11: Multilayered nanoparticles for cancer therapy



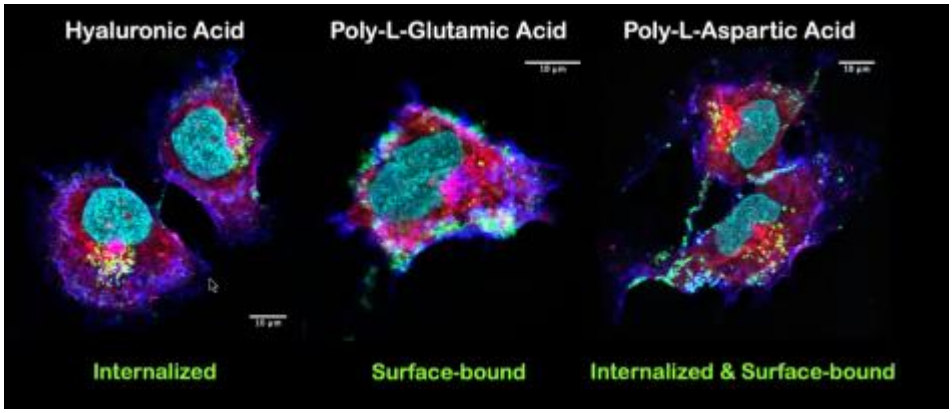
Source: Hammond, MIT Women in Biotech, 2021

LbL nanoparticles can be constructed on any core nanoparticles, for instance lipid nanoparticles, to deliver anti-tumor cargo like chemotherapy. Additionally, The LbL nanoparticle system can be further modified to include additional anti-tumor mechanisms. One approach is by using siRNA (embedded in the negatively charged layer) to overcome the tumor defensive mechanisms. As the content of each layer of LbL nanoparticles is released in sequence, the siRNA will be released to the tumor or tumor microenvironment prior to chemotherapy, thus optimizing the tumor clearance. It wouldn't be surprising to see different interactions between layers and different anti-tumor mechanisms can be customer-tailored to address different types of tumors in the clinic.

The Hammond lab also found coating of the outer layer may affect the delivery and distribution of LbL nanoparticles. For instance, nanoparticles with hyaluronic acid (HA) on the outer layer bind to tumor cells with high specificity through the interaction of HA with the CD44 receptor, allowing a more targeted delivery of chemotherapy without systemic toxicity. The HA LbL nanoparticles have been tested in several in vivo models including NSCLC. Treatment with HA LbL nanoparticles (contain KRAS siRNA + miR34a microRNA in the LbL film, and cisplatin in the core) led to superior survival benefits in vivo compared to RNA-only or cisplatin-only treatments.

The outer layer can also "steer" the LbL nanoparticles to different parts of the cell. While HA-coated LbL nanoparticles lead to significant levels of cell internalization that is ideal for direct tumor-killing, PLE-coated nanoparticles will mostly bind to the cell surface, providing an alternative route for cancer treatment by delivering cargo to the tumor microenvironment. An emerging research area exploiting PLE LbL nanoparticles is to deliver cytokines into the tumor microenvironment to turn "cold" tumors into "hot" tumors. The lab is testing the delivery of IL-12 using such an approach. Preliminary in vivo results show the PLE-IL-12 is less toxic than naïve IL-12, which often leads to systemic toxicity and body weight loss. PLE-IL-12 particles also localize immune cell activation to tumors and cause substantial PD-L1 expression upregulation in tumors.

Exhibit 12. The outer layer can steer the LbL nanoparticles to different parts of the cell



Source: Hammond, MIT Women in Biotech, 2021

Stock prices of other companies mentioned in this report (as of 8/17/2021):

Daré Bioscience, Inc. (DARE-NASDAQ; $1.48; Not Covered)

Lyra Therapeutics, Inc. (LYRA-NASDAQ; $6.85; Not Covered)

Kronos Bio Inc (KRON-NASDAQ; $19.53; Not Covered)

PureTech Health PLC Sponsored ADR (PRTC-NASDAQ; $47.64; Not Covered)

Disclosure Appendix

Oppenheimer & Co. Inc. does and seeks to do business with companies covered in its research reports. As a result, investors should be aware that the firm may have a conflict of interest that could affect the objectivity of this report. Investors should consider this report as only a single factor in making their investment decision.

Analyst Certification - The author certifies that this research report accurately states his/her personal views about the subject securities, which are reflected in the ratings as well as in the substance of this report. The author certifies that no part of his/her compensation was, is, or will be directly or indirectly related to the specific recommendations or views contained in this research report.

Potential Conflicts of Interest:

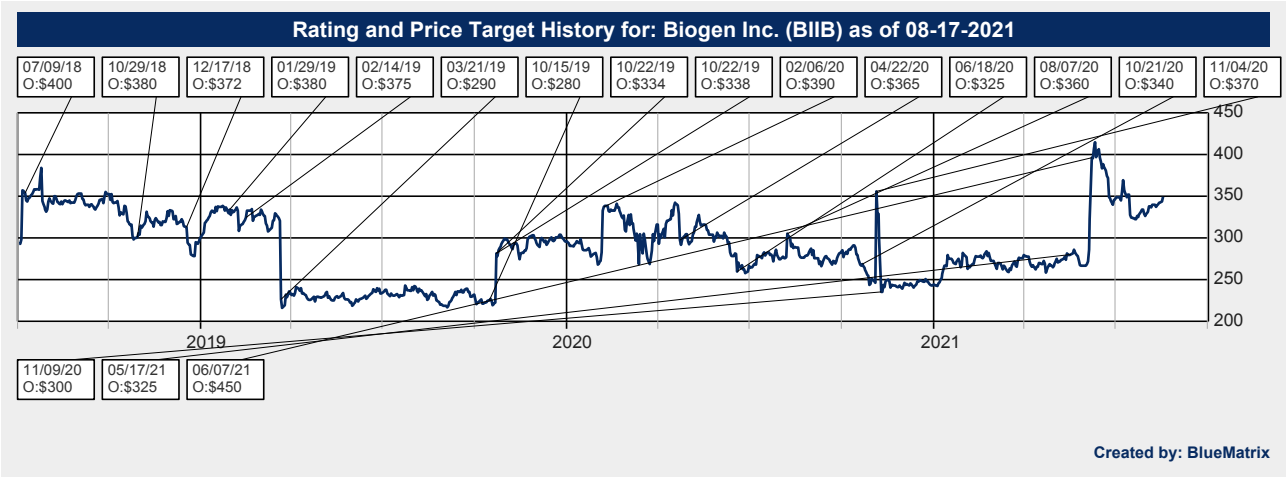
Equity research analysts employed by Oppenheimer & Co. Inc. are compensated from revenues generated by the firm including the Oppenheimer & Co. Inc. Investment Banking Department. Research analysts do not receive compensation based upon revenues from specific investment banking transactions. Oppenheimer & Co. Inc. generally prohibits any research analyst and any member of his or her household from executing trades in the securities of a company that such research analyst covers. Additionally, Oppenheimer & Co. Inc. generally prohibits any research analyst from serving as an officer, director or advisory board member of a company that such analyst covers. In addition to 1% ownership positions in covered companies that are required to be specifically disclosed in this report, Oppenheimer & Co. Inc. may have a long position of less than 1% or a short position or deal as principal in the securities discussed herein, related securities or in options, futures or other derivative instruments based thereon. Recipients of this report are advised that any or all of the foregoing arrangements, as well as more specific disclosures set forth below, may at times give rise to potential conflicts of interest.

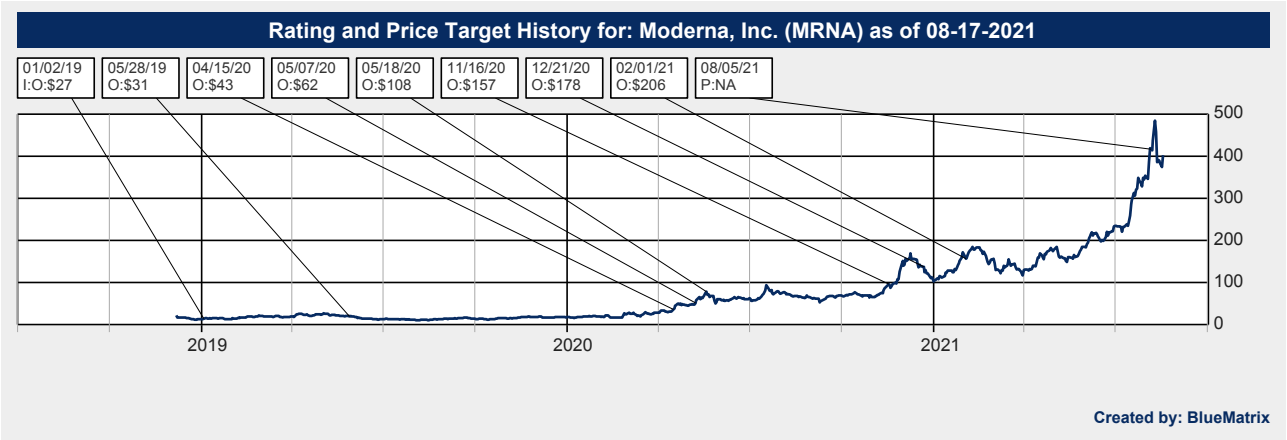
Important Disclosure Footnotes for Companies Mentioned in this Report that Are Covered by Oppenheimer & Co. Inc:

Stock Prices as of August 18, 2021

Biogen Inc. (BIIB - NASDAQ, $349.79, OUTPERFORM)

Moderna, Inc. (MRNA - NASDAQ, $401.86, PERFORM)





All price targets displayed in the chart above are for a 12- to- 18-month period. Prior to March 30, 2004, Oppenheimer & Co. Inc. used 6-, 12-, 12- to 18-, and 12- to 24-month price targets and ranges. For more information about target price histories, please write to Oppenheimer & Co. Inc., 85 Broad Street, New York, NY 10004, Attention: Equity Research Department, Business Manager.

Oppenheimer & Co. Inc. Rating System as of January 14th, 2008:

Outperform(O) - Stock expected to outperform the S&P 500 within the next 12-18 months.

Perform (P) - Stock expected to perform in line with the S&P 500 within the next 12-18 months.

Underperform (U) - Stock expected to underperform the S&P 500 within the next 12-18 months.

Not Rated (NR) - Oppenheimer & Co. Inc. does not maintain coverage of the stock or is restricted from doing so due to a potential conflict of interest.

Oppenheimer & Co. Inc. Rating System prior to January 14th, 2008:

Buy - anticipates appreciation of 10% or more within the next 12 months, and/or a total return of 10% including dividend payments, and/or the ability of the shares to perform better than the leading stock market averages or stocks within its particular industry sector.

Neutral - anticipates that the shares will trade at or near their current price and generally in line with the leading market averages due to a perceived absence of strong dynamics that would cause volatility either to the upside or downside, and/or will perform less well than higher rated companies within its peer group. Our readers should be aware that when a rating change occurs to Neutral from Buy, aggressive trading accounts might decide to liquidate their positions to employ the funds elsewhere.

Sell - anticipates that the shares will depreciate 10% or more in price within the next 12 months, due to fundamental weakness perceived in the company or for valuation reasons, or are expected to perform significantly worse than equities within the peer group.

Distribution of Ratings/IB Services Firmwide

			IB Serv/Past 12 Mos.	
Rating	Count	Percent	Count	Percent
OUTPERFORM [O]	466	69.97	255	54.72
PERFORM [P]	200	30.03	75	37.50
UNDERPERFORM [U]	0	0.00	0	0.00

Although the investment recommendations within the three-tiered, relative stock rating system utilized by Oppenheimer & Co. Inc. do not correlate to buy, hold and sell recommendations, for the purposes of complying with FINRA rules, Oppenheimer & Co. Inc. has assigned buy ratings to securities rated Outperform, hold ratings to securities rated Perform, and sell ratings to securities rated Underperform.

Note: Stocks trading under $5 can be considered speculative and appropriate for risk tolerant investors.

Company Specific Disclosures

In the past 12 months Oppenheimer & Co. Inc. has received compensation for investment banking services from MRNA.

Additional Information Available

Company-Specific Disclosures: Important disclosures, including price charts, are available for compendium reports and all Oppenheimer & Co. Inc.-covered companies by logging on to https://www.oppenheimer.com/client-login.aspx or writing to Oppenheimer & Co. Inc., 85 Broad Street, New York, NY 10004, Attention: Equity Research Department, Business Manager.

Other Disclosures

This report is issued and approved for distribution by Oppenheimer & Co. Inc. Oppenheimer & Co. Inc. transacts business on all principal exchanges and is a member of SIPC. This report is provided, for informational purposes only, to institutional and retail investor clients of Oppenheimer & Co. Inc. and does not constitute an offer or solicitation to buy or sell any securities discussed herein in any jurisdiction where such offer or solicitation would be prohibited. The securities mentioned in this report may not be suitable for all types of investors. This report does not take into account the investment objectives, financial situation or specific needs of any particular client of Oppenheimer & Co. Inc. Recipients should consider this report as only a single factor in making an investment decision and should not rely solely on investment recommendations contained herein, if any, as a substitution for the exercise of independent judgment of the merits and risks of investments. The analyst writing the report is not a person or company with actual, implied or apparent authority to act on behalf of any issuer mentioned in the report. Before making an investment decision with respect to any security recommended in this report, the recipient should consider whether such recommendation is appropriate given the recipient's particular investment needs, objectives and financial circumstances. We recommend that investors independently evaluate particular investments and strategies, and encourage investors to seek the advice of a financial advisor. Oppenheimer & Co. Inc. will not treat non-client recipients as its clients solely by virtue of their receiving this report. Past performance is not a guarantee of future results, and no representation or warranty, express or implied, is made regarding future performance of any security mentioned in this report. The price of the securities mentioned in this report and the income they produce may fluctuate and/or be adversely affected by exchange rates, and investors may realize losses on investments in such securities, including the loss of investment principal. Oppenheimer & Co. Inc. accepts no liability for any loss arising from the use of information contained in this report, except to the extent that liability may arise under specific statutes or regulations applicable to Oppenheimer & Co. Inc. All information, opinions and statistical data contained in this report were obtained or derived from public sources believed to be reliable, but Oppenheimer & Co. Inc. does not represent that any such information, opinion or statistical data is accurate or complete (with the exception of information contained in the Important Disclosures section of this report provided by Oppenheimer & Co. Inc. or individual research analysts), and they should not be relied upon as such. All estimates, opinions and recommendations expressed herein constitute judgments as of the date of this report and are subject to change without notice. Nothing in this report constitutes legal, accounting or tax advice. Since the levels and bases of taxation can change, any reference in this report to the impact of taxation should not be construed as offering tax advice on the tax consequences of investments. As with any investment having potential tax implications, clients should consult with their own independent tax adviser. This report may provide addresses of, or contain hyperlinks to, Internet web

sites. Oppenheimer & Co. Inc. has not reviewed the linked Internet web site of any third party and takes no responsibility for the contents thereof. Each such address or hyperlink is provided solely for the recipient's convenience and information, and the content of linked third party web sites is not in any way incorporated into this document. Recipients who choose to access such third-party web sites or follow such hyperlinks do so at their own risk.

This research is distributed in the UK and elsewhere throughout Europe, as third party research by Oppenheimer Europe Ltd, which is authorized and regulated by the Financial Conduct Authority (FCA). This research is for information purposes only and is not to be construed as a solicitation or an offer to purchase or sell investments or related financial instruments. This research is for distribution only to persons who are eligible counterparties or professional clients. It is not intended to be distributed or passed on, directly or indirectly, to any other class of persons. In particular, this material is not for distribution to, and should not be relied upon by, retail clients, as defined under the rules of the FCA. Neither the FCA's protection rules nor compensation scheme may be applied. https://opco2.bluematrix.com/sellside/MAR.action

Distribution in Hong Kong: This report is prepared for professional investors and is being distributed in Hong Kong by Oppenheimer Investments Asia Limited (OIAL) to persons whose business involves the acquisition, disposal or holding of securities, whether as principal or agent. OIAL, an affiliate of Oppenheimer & Co. Inc., is regulated by the Securities and Futures Commission for the conduct of dealing in securities and advising on securities. For professional investors in Hong Kong, please contact researchasia@opco.com for all matters and queries relating to this report. This report or any portion hereof may not be reprinted, sold, or redistributed without the written consent of Oppenheimer & Co. Inc.

This report or any portion hereof may not be reprinted, sold, or redistributed without the written consent of Oppenheimer & Co. Inc. Copyright © Oppenheimer & Co. Inc. 2021.